all of which enhance the vitamin D status, were found to be effective measures in treating tuberculosis more than 100 years ago. Recent evidence suggests that improvement in vitamin D status reduces risk for upper respiratory tract infections including influenza A infection by more than 40% [9].

The comment about whether a single "biochemical marker can provide meaningful insight into the health status of an individual" overlooks the fact that skin pigmentation varies globally according to solar UV doses; dark enough to reduce the risk for free radical production and DNA damage and folate destruction, yet light enough to permit vitamin D production [10].

As to the higher prevalence of low serum 25(OH)D concentrations among the oldest old, a little known fact is that the prevalence of people with apolipoprotein epsilon4 (ApoE4) decreases with advanced age [11] and ApoE4 is associated with higher serum 25(OH)D concentrations [12].

There is strong evidence that vitamin D reduces the risk for other diseases that are important causes of premature death: cardiovascular disease [13], and type 2 diabetes mellitus [14]. Based on serum 25(OH)D concentration–health outcome relations, it was estimated that if population mean serum 25(OH)D concentrations were raised from 54 nmol/L to 110 nmol/L in developed countries, mortality rates would decrease by 15% to 20% and life expectancy would increase by 2 y [15]. The demonstrated benefits of increasing serum 25(OH)D concentrations greatly outweigh any hypothetical risks in doing so.

References

[1] Glade MJ. Vitamin D: Health panacea or false prophet? Nutrition 2013;29:37–41.
[2] Grant WB. Ecological studies of the UVB–vitamin D–cancer hypothesis; review. Anticancer Res 2012;32:223–36.
[3] Grant WB, Peiris AN. Differences in vitamin D status may account for unexplained disparities in cancer survival rates between African and White Americans. Dermatoendocrinol 2012;4:85–94.
[4] Grant WB. Role of solar UV irradiance and smoking in cancer as inferred from cancer incidence rates by occupation in Nordic countries. Dermatoendocrinol 2012;4:203–11.
[5] Hill AB. The environment and disease: Association or causation? Proc R Soc Med 1965;58:295–300.
[6] Grant WB. How strong is the evidence that solar ultraviolet B and vitamin D reduce the risk of cancer? An examination using Hill's criteria for causality. Dermatoendocrinol 2009;1:17–24.
[7] Mohr SB, Gorham ED, Alcaraz JE, Kane CI, Macera CA, Parsons JE, et al. Does the evidence for an inverse relationship between serum vitamin D status and breast cancer risk satisfy the Hill criteria? Dermatoendocrin 2012;4:152–7.
[8] Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266–81.
[9] Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y, Ida H. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am J Clin Nutr 2010;91:1255–60.
[10] Jablonski NG, Chaplin G. Colloquium paper: human skin pigmentation as an adaptation to UV radiation. Proc Natl Acad Sci U S A 2010;107(suppl 2):8962–8.
[11] Kulminski AM, Culminskaya I, Ukraintseva SV, Arbeev KG, Arbeeva L, Wu D, et al. Trade-off in the effects of the apolipoprotein E polymorphism on the ages at onset of CVD and cancer influences human lifespan. Aging Cell 2011;10:533–41.
[12] Huebbe P, Nebel A, Siegert S, Moehring J, Boesch-Saadatmandi C, Most E, et al. APOE ε4 is associated with higher vitamin D levels in targeted replacement mice and humans. FASEB J 2011;25:3262–70.
[13] Wang L, Song Y, Manson JE, Pilz S, März W, Michaëlsson K, et al. Circulating 25-hydroxy-vitamin D and risk of cardiovascular disease: A meta-analysis of prospective studies. Circ Cardiovasc Qual Outcomes 2012;5:819–29.
[14] Afzal S, Bojesen SE, Nordestgaard BG. Low 25-hydroxyvitamin D and risk of type 2 diabetes: A prospective cohort study and meta-analysis. Clin 2013;59:381–91.
[15] Grant WB. An estimate of the global reduction in mortality rates through doubling vitamin D levels. Eur J Clin Nutr 2011;65:1016–26.

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Vitamin D: Let's just ask the right questions. A response to Grant and Holick

To the Editor:

The letter from Drs. Grant and Holick, submitted in response to my review [1], presents a well-reasoned argument supporting the "health panacea" hypothesis. However, they may have missed both the import of the paper as well as an opportunity. The "take-home" message was that epidemiology, as with all research, is able to answer only those questions that are asked. It has not addressed, at least not yet, the issues that are raised in my review about the specific potential downsides or unsuspected pitfalls of universally increasing vitamin D intake from youth into old age. In this context, their argument fails to reconcile the current conflicts between population-based health policies and the individualization of nutritional advice and care.

The potential roles of the Klotho system in altering human longevity deserve better treatment than was afforded the "nonskeletal" benefits of increased vitamin D intake during the past century. In the 21st century, nutrition science must probe beyond the conceptual limitations of the 20th century, no matter how frustrating it may be that those limitations continue to constrain public health policy, in order to advance every individual's opportunity to benefit from nutritional wisdom regarding disease prevention, health maintenance, and the pursuit of human happiness.

Reference

[1] Glade MJ. Vitamin D: Health panacea or false prophet? Nutrition 2013;29:37–41.

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